Granular cell tumour of the common bile duct

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Summary: Granular cell tumours are a rare cause of benign biliary stricture. A case is reported which is unusual in that the diagnosis was made before the onset of jaundice. We emphasize the importance of accurate histology of biliary strictures, to eliminate confusion between those of benign and malignant nature and to ensure that the appropriate management is undertaken. Immunohistochemical evidence for the neural origin of this rare tumour is presented.

Introduction

Granular cell tumours (GCT) are uncommon benign lesions whose histogenesis has remained obscure since their description by Abrikossoff in 1926. Their occurrence in the extrahepatic biliary tree is rare and of the 33 cases so far described, only 3 have been reported in the British literature (Savage & Devitt, 1977; Dewar *et al.*, 1981; Barber, 1984). A granular cell tumour of the common bile duct is described which is unusual in that the diagnosis was made before the onset of jaundice.

Case report

A 38 year old Caucasian woman presented with a one year history of recurrent attacks of colicky, right hypochondrial pain each lasting several hours. There was no history of jaundice and examination was unremarkable.

An oral cholecystogram failed to opacify the gall bladder but ultrasound examination of the gall bladder was normal. Liver function tests performed shortly after an attack of pain showed: alkaline phosphatase 345 IU/l (normal 30–110 IU/l), aspartate transaminase 99 IU/l (normal 5–40 IU/l) and bilirubin 15 μ mol/l (normal 5–17 μ mol/l). In the absence of gallstones and with abnormal liver function tests bile duct obstruction was suspected. Endoscopic retrograde cholangiopancreatography (ERCP) showed a tight stricture in the mid-portion of the bile duct, absent filling of the

cystic duct and dilatation of the biliary tree above the stricture (Figure 1).

A malignant bile duct stricture was suspected and at laparotomy a 1 cm firm nodule was found in the

Figure 1 ERCP showing a tight stricture in the mid-portion of the bile duct, absent filling of the cystic duct and dilatation of the biliary tree above the stricture.

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common bile duct at its junction with the cystic and common hepatic ducts. The common hepatic duct was dilated and the gall bladder collapsed. The nodule was resected with a cuff of normal bile duct, cystic duct and gall bladder and a Roux-en-Y hepato-jejunostomy performed. The patient made an uncomplicated recovery and remains well 2 years later.

Pathology

A firm nodule measuring 1 cm in diameter with a yellow-white cut surface was noted within the wall of the common bile duct almost occluding its lumen and completely obstructing the cystic duct. The gall bladder was normal and did not contain stones. Histologically, the lesion did not appear encapsulated and was composed of clumps of large cells with distinct cell boundaries, small dark round nuclei and eosinophilic granular cytoplasm. These are the features of a granular cell tumour.

In some areas the tumour cells were closely associated with nerve bundles of an unusually large size for the biliary tree. The tumour cells showed staining for S-100 protein, neurone-specific enolase (NSE) (Figure 2) and PGP 9.5. S-100 protein is a marker for Schwann cells, Langerhans cells and cartilage whilst NSE and PGP 9.5 are markers for neural and neuroendocrine tissue. Staining of the tumour cells with these markers provides evidence for the neural origin of GCT.

Discussion

Benign tumours of the extrahepatic biliary tree are uncommon and are usually epithelial (papillomas and adenomas) or predominantly epithelial (adenomyomas and polyps). Granular cell tumours at this site are rare. There have been 33 cases reported including 16 in the common bile duct (Figure 3). A review of these cases shows that GCT of the extrahepatic biliary tree occurs almost exclusively in women (94%) and usually presents in the third to fifth decades. It appears to be more common in negroes as is true of GCT found at other sites (Lack *et al.*, 1980). GCT is occasionally multiple: one patient had multiple tumours in the biliary tree (Aisner *et al.*, 1982) and four had tumours elsewhere (Assor, 1979; Manstein *et al.*, 1981; Livolsi *et al.*, 1973).

The clinical features of granular cell tumour resemble those of both malignant bile duct strictures and gallstones. The benign nature of this tumour may be suspected at operation but confirmation of the diagnosis depends on histological examination of the resected specimen. Except for two tumours found at post-mortem (Coggins, 1952; Whitmore *et al.*, 1969)

Figure 2 Granular cell tumour of the wall of the common bile duct immunostained for neurone-specific enolase. Tumour cells with abundant granular cytoplasm are seen staining darkly beneath the surface epithelium (upper part) and around glands of the bile duct – $\times 110$. *Inset:* High power view of neurone-specific enolase positive tumour cells within and around the perineurium of a small nerve, $\times 230$.

all previously reported lesions have been successfully treated surgically.

GCT is much more common at sites outside the biliary tree and has been described in most parts of the body. The commonest sites are the skin, subcutaneous tissues, oral cavity and tongue (Lack *et al.*, 1980). At certain sites such as the biliary tract, bronchus (Garancis *et al.*, 1970), vocal cord or oesophagus (Mauro & Jacques, 1981) GCT can produce significant symptoms and may be mistaken for a malignant lesion.

Figure 3 Distribution of GCT in the extrahepatic biliary tree. GB = gall bladder, D = duodenum, P = pancreas, (+) = multiple tumours in one patient.

The histogenesis of GCT is unclear, a neural origin being the most widely accepted view at present. These tumours are often closely associated with nerves and occasionally wholly confined within a nerve (Bangle,

1953). GCT cells contain granules resembling the secretory granules characteristic of neural cells and show immunohistochemical staining for the Schwann cell marker S-100 protein (Dhillon & Rode, 1983) and the neural markers PGP 9.5 and NSE (Rode *et al.*, 1982, 1985). A Schwann cell origin has been proposed (Fischer & Wechsler, 1962) but more recently Rode *et al.* (1982) suggested that this tumour arises from an undifferentiated precursor cell which has the capacity to differentiate into either Schwann or GCT cells.

Granular cell tumour is a rare, benign lesion which may cause bile duct obstruction and should be considered in the differential diagnosis of biliary pain with or without jaundice. Accurate histology of biliary strictures is important to eliminate confusion between those of benign and malignant nature and to ensure that the appropriate management is undertaken.

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